indicated. **(D)** PCR genotyping of embryos. Two allele, three primer PCR was performed on genomic DNA from E18.5 embryos isolated from GRHL-3+/- intercrosses. The size of DNA standards (in bp) is indicated target, PCR product diagnostic of targeted 25 GRHL-3 allele; wt. PCR product diagnostic of wild type GRHL-3 allele. ~~**(E) Northern blot analysis of GRHL-3 mRNA expression in wild type embryos and embryos heterozygous or homozygous for the targeted GRHL-3 allele (upper panel). RNA integrity was confirmed with a GAPDH probe (lower panel). The size of RNA standards is indicated, as is the migration of the GRHL-3 and GAPDH transcripts. (F) RT-PCR of E9.5 GRHL-3$^{-/-}$ and GRtIL-3$^{+/-}$ embryos was performed with primers specific for HPRT. Based on the HPRT quantitation, comparable amounts of cDNA from each embryo were PCR amplified for 30, 32 and 35 cycles (GRHL-3$^{+/-}$) or 35, 38 and 40 cycles (GRHL-3$^{-/-}$) with primers specific for GRHL-3. The 5' primer anneals to exon 8 and the 3' primer anneals to exon 13. Both primer pairs gave predicted size bands of 503 bp for GRHL-3 and 229 bp for HPRT. The identities of the amplified bands were confirmed by Southern blotting using gene specific internal oligonucleotides.**~~

Please replace the paragraph spanning pages ~~14-15~~ 15-16 of the Specification under the header "BRIEF DESCRIPTION OF THE FIGURES" with the following paragraph:

Figure 7 is a representation showing GRHL-3 and ct are the same gene. **(A)** Organization 20 of the ct candidate region. Genetic map of the 13 Mb supercontig (Accession number NW_000213) that shows the positions of relevant markers (D4Mit69 and D4Mit157) and previously excluded ct candidate genes (*Synd3*, *Fgr*, *Hspg2*, *Pax7*). The position of the GRHL-3 locus is also indicated. The size of the interval between the GRHL-3 locus and the D4Mit69 marker is shown. **(B)** Morphological appearance and genotype of embryos derived from ct/ct mice crossed with GRHL-3$^{+/-}$ mice. Embryo 1 is unremarkable; embryos 2 and 3 display curly tails (arrowheads); embryos 4 and 5 display curly tails and lumbo-sacral spine bifida (arrows). ct. curly tail; SB, spine bifida. Scale bar = 10mm. **(C)** Total RNA from E14.5 embryos from *curly tail* (*ct/ct*), wild type (+/+) and GRHL-3 heterozygotes (+/-) were analysed for GRHL-3 expression by Northern blotting with a cDNA probe derived from the unique coding portion of the mRNA described in Fig 1A (upper panel). RNA loading was monitored by probing with 28S (lower panel). Signal intensity was quantified by Phosphorimager densitometry and the individual embryo GRHL-3 signals corrected for 28S loading. The corrected signal intensities relative to wild type embryo 7

are shown. Positions of GRHL-3, 28S and the RNA size standards are indicated. **(D)** Quantitative real-time RT-PCR was performed on total RNA from E14.5 5 *curly tail* (*ct/ct*), wild type (+/+) and GRHL-3 heterozygous (+/-) embryos. A standard curve was generated for HPRT and GRHL-3 and the relative quantity of both transcripts was calculated for individual embryos. Each reaction was performed in duplicate. The ratios of GRHL-3/HPRT in GRHL-$3^{+/-}$ and *ct/ct* embryos were normalised to the values obtained with GRHL-$3^{+/+}$ embryos. (E) Northern blot analysis of GRHL-3 mRNA expression in wild type embryos and embryos heterozygous or homozygous for the targeted GRHL-3 allele (upper panel). RNA integrity was confirmed with a GAPDH probe (lower panel). The size of RNA standards is indicated, as is the migration of the GRHL-3 and GAPDH transcripts. **(F)** RT-PCR of E9.5 GRHL-$3^{-/-}$ and GRtIL-$3^{+/-}$ embryos was performed with primers specific for HPRT. Based on the HPRT quantitation, comparable amounts of cDNA from each embryo were PCR amplified for 30, 32 and 35 cycles (GRHL-$3^{+/-}$) or 35, 38 and 40 cycles (GRHL-$3^{-/-}$) with primers specific for GRHL-3. The 5' primer anneals to exon 8 and the 3' primer anneals to exon 13. Both primer pairs gave predicted size bands of 503 bp for GRHL-3 and 229 bp for HPRT. The identities of the amplified bands were confirmed by Southern blotting using gene-specific internal oligonucleotides.

Please replace the paragraph on page 78 of the Specification under the header "EXAMPLE 16" with the following paragraph:

Amw 4/16/08

To determine the functional role of GRHL-3 during mouse development, a 2.2 kb deletion in GRHL-3 was generated by gene targeting (Fig. 5A-D). Northern blot and RT-PCR analysis indicated that the targeted GRHL-3 allele represented a null mutation (Fig. 7E and F~~5E,F~~). Genotyping of offspring from GRHL-$3^{+/-}$ intercrosses from mid and late gestation, showed that GRHL-$3^{-/-}$ mice were represented in Mendelian proportions up to E18.5. Of 874 embryos examined on, or before this time, 191 (22%) were genotyped as GRHL-$3^{-/-}$. No GRHL-$3^{-/-}$ embryos survived to weaning.